REMARKS

Reconsideration is requested.

Claims 1-16, 21, 31 and 39 have been canceled, without prejudice. Claims 17-20, 22-30 and 32-38 are pending.

The Examiner is requested to forward a PTO 892 Form listing the cited Klem (U.S. Patent Application Publication No. 2003/0176376) and Opalinska et al "Nucleic-acid Therapeutics: Basic Principles and Recent Applications" Nature Reviews, Volume.1, July 2002, pages 503-514. The former having been applied by the Examiner as a basis of a rejection in the Office Action of August 28, 2008 and the latter being contained in the PTO IFW.

The objection to claim 21 is moot in view of the above. The objections to claims 25, 26, 27 and 29 are obviated by the above amendments.

The Section 112, first paragraph "written description", rejection of claims 28 and 29 is obviated by the above amendments. The claims are supported by an adequate written description. Claims 28 and 29 have been revised, without prejudice, to delete the objected-to phrases in order to advance prosecution. Withdrawal of the Section 112, first paragraph "written description", rejection is requested.

The Section 103 rejection of claims 17-27, 30 and 32-38 over the combination of Omori (DNA Repair, Elsevier, Amsterdam, NL, 2002, pp 299-310), Marthinet (Gene Therapy 2000, Vol. 7, pp 1224-1233) and Klem (U.S. Patent Application Publication No. 2003/0176376), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Neither Marthinet et al nor Klem et al teach or suggest the use of a decoy according to the present invention. Marthinet et al is understood to teach that double-stranded oligonucleotides reproducing *cis*-regulatory elements of MED-1 of MDR1 gene can be used in a strategy targeting a gene. This is a transcriptional decoy strategy (see page 1228, right col. 1st ¶ of Discussion section of Marthinet et al). Klem et al, is understood by the applicants to use the same strategy as Marthinet et al, i.e., transcriptional decoy strategy targeting CRE enhancer sequence.

This transcriptional decoy strategy is different from the strategy of the invention because the goal of the decoy approach developed by Martinet and Klem is to decrease the level of gene transcription by trapping transcription factors essential to activate transcriptional complexes specific of these genes or class of genes.

In the present invention, the molecules are not decoy molecules of transcriptional factors because they render Ku protein unavailable to take part in the early stage of DNA double strand break repair. The important feature is the ability of the molecules to be bound by the Ku protein involved in the NHEJ pathway of double strand breaks repair. The effect of the molecules of the present invention is independent from their sequence as noted in the specification (see for example, page 5, lines 16-20 and page 33, lines 11-12 of the present specification).

Accordingly, the molecules of the present invention do not modify the Ku gene and protein expression as suggested by Omori et al, and the molecules of the invention do not need to have an homology with the regulatory element of the gene encoding Ku protein.

In addition, the person of ordinary skilled in art wishing to decrease the Ku70 expression by the transcriptional decoy strategy, would not have found the teachings of Marthinet et al and Klem et al as not suggestive or applicable to Ku70 protein because the transcriptional decoy strategy requires the presence of specific transcriptional elements to be targeted. Specifically, in Marthinet et al, the decoy targets MED-1 element of MDR1 gene. This is a situation specific of this gene in cancer cells.

In this gene, the MED-1 element has a particular structure (see page 1224, right col., 1st ¶ : "*In the human TATA-less MDR1 gene promoter, the consensus MED-1 sequence (GGGAGC) is reversed compared with that in the TATA-less hamster pgp1 promoter (GCTCC(C/G)), and is located upstream of the transcription start points.*"). In addition, the use of this structure is specific to PgP-overproducing cancer cells (see page 1224, right col., 1st ¶ : "*Wild-type, Pgp-producing cells use a single transcriptional start site whereas Pgp-overproducing cancer cells (without gene amplification) use multiple start sites.*"). Finally, this target can produce a specific effect (see page 1224, right col., 1st ¶ : "*Analysis of the pattern of multiple start sites in TATA-less promoters, revealed that inactivation of the downstream MED-1 element decreased the frequency of initiation from the multiple start points while initiation from the upstream start site remained unaffected*"). The specificity of the strategy is also underlined in the Discussion section (see page 1228, right col, 3rd ¶ of Discussion section (emphasis added): "*To develop the transcriptional decoy strategy described here we took advantage of the specificity of the MDR1 gene promoter found in MDR cancer cells: (…). The resulting configuration is unique to the human MDR1 gene as represented in*

Figure 7."; page 1229, left col., 4th ¶ (emphasis added) : "*The human MDR1 gene is rather special in its class of TATA-less promoter genes (…), the human MED-1 cis-element that is present in Pgp overexpressing cancer cells represents a valuable potential specific target for anti-gene and gene therapy approaches.*"; page 1229, right col., 1st ¶ (emphasis added): "*the configuration of the human MED-1 cis-element is unique to the human Pgp over-producing cells*"; and page 1229, right col., 3rd ¶ (emphasis added) : "*The human MED-1 element found in the MDR1 gene represents a particular case for different reasons*").

Similarly, in Klem et al, oligomers target CRE enhancer for binding to transcription factors, thereby altering the expression of genes containing CRE enhancer regulatory sequences (see ¶ [0006]). Accordingly, there is also a specific target. The specificity results in specificity in the effect (see ¶ [0007] "Thus, CRE decoy oligomers can be useful for inhibiting cancer cell growth, without adversely affecting the growth of noncancerous cells").

In the case of Ku70, Omori et al teach an antisense strategy, the sole requirement of which being to know the mRNA sequence to target. However, none of the cited document teaches specific transcriptional elements that can be used in the transcriptional decoy strategy to specifically decrease the expression of Ku70.

None of the cited documents teach or suggest, individually or in combination, the strategy of the present invention to trap the Ku protein in order to render them unavailable for the DNA repair. The teaching of Omori et al would not have been combined with the teachings of Marthinet et al or Klem et al because, for example, of

the lack of teaching of specific transcriptional elements to be targeted for a specific impact on Ku70 expression.

The claimed invention would not have been obvious in view of the cited combination of art. Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required to obtain allowance.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100